

# PATENT SPECIFICATION

NO DRAWINGS

887,411



Date of Application and filing Complete Specification: May 23, 1958.

No. 16587/58.

Application made in United States of America on May 31, 1957.

Complete Specification Published: Jan. 17, 1962.

Index at acceptance:—Classes 2(3), C2B20; and 81(1), E1C3B3.

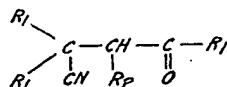
International Classification:—C07c. A01n.

## COMPLETE SPECIFICATION

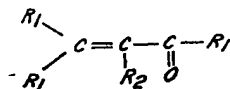
### Preparation of $\beta,\beta$ -Disubstituted- $\beta$ -Cyanoketones

We, ROHM & HAAS COMPANY, a corporation organized under the laws of the State of Delaware, United States of America, of 222 West Washington Square, Philadelphia 5, Pennsylvania, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention is concerned with a process for the preparation of a  $\beta,\beta$ -disubstituted- $\beta$ -cyanoketone of the formula:



by the hydrocyanation of a  $\beta,\beta$ -disubstituted- $\alpha,\beta$ -unsaturated ketone of the formula:



wherein, in the above formulae,  $R_1$  represents a methyl or ethyl group,  $R_2$  represents hydrogen or a methyl or ethyl group, the  $R_1$  substituents being the same or different and the  $R_1$  and  $R_2$  substituents being such that the nitrile product contains from 7 to 9 carbon atoms.

In accordance with this invention, it has been found that good yields of a cyanoketone as defined above can be obtained by carrying out the hydrocyanation of the unsaturated ketone under certain specific conditions set forth below.

In the first place, the hydrocyanation reaction is carried out at a superatmospheric pressure and at a temperature which is at least 130°C. but which does not exceed 350°C.

Secondly the reaction is initiated by bringing

[Pri

together, at the reaction temperature, pre-formed mixtures of (a) an alkaline catalyst capable of generating cyanide ions and said  $\alpha,\beta$ -unsaturated ketone reactant or the desired cyanoketone product and (b) hydrocyanic acid and said  $\alpha,\beta$ -unsaturated ketone reactant. Finally, the hydrocyanic acid mixture (b) is gradually brought into contact with the catalyst mixture (a) at a rate which is substantially that at which the hydrocyanic acid reacts with the ketone.

Typical of the  $\beta,\beta$ -disubstituted- $\alpha,\beta$ -unsaturated ketone reactants that may be employed are 4 - methyl - 3 - penten - 2 - one, 4 - methyl - 3 - hexen - 2 - one, 2 - methyl - 2-hexen-4-one, 2-methyl-2-hepten-4-one, 3-methyl - 3 - hepten - 5 - one, 3,4-dimethyl - 3 - penten - 2 - one, 3,4 - dimethyl - 3-hexen - 2 - one, 4,5 - dimethyl - 4 - hexen - 3-one, and 3-ethyl-3-hexen-2-one.

The  $\alpha,\beta$ -unsaturated ketone reactant employed in the process of the invention frequently exists in the form of a mixture with the corresponding  $\beta,\gamma$ -unsaturated tautomer(s). The  $\beta,\gamma$ -unsaturated compounds will themselves, in the presence of basic compounds, form mixtures of  $\alpha,\beta$ - and  $\beta,\gamma$ -unsaturated tautomers and can therefore be used as a source of the  $\alpha,\beta$ -unsaturated tautomer. Such a mixture can be employed in the process and the term  $\alpha,\beta$ -unsaturated ketone reactant used herein is to be construed as embracing such tautomeric mixtures.

The process of the invention may be carried out in a batchwise or continuous fashion, as desired. When the reaction is conducted in a batchwise fashion, temperatures in the range of 130°C. to 275°C. are generally employed, with a range of 130° to 220°C. preferred. Temperatures appreciably below 100°C. lead to insignificant or undesirable results, if any at all. Temperatures appreciably above 275°C. may lead to undesired decompositions.

Pressures from 25 to 250 psig are advantageously employed in batchwise operations. The exact pressure used may be determined

to a certain extent by the boiling point of the ketone reactant concerned, when the pressure used is that which is autogenously produced at the reaction temperatures. Specifically, for instance, the lowest molecular weight ketone reactant contemplated, mesityl oxide, will produce autogenous pressures of about 25 to 250 pounds per square inch gauge at the preferred reaction temperatures defined.

If the present reaction is conducted on a continuous basis, temperatures up to 350° C. may be employed, particularly if contact times are limited to 10 to 20 minutes. Particularly advantageous is a temperature range of 200° to 240° C. with contact times of 10 to 12 minutes. Also, at the defined reaction temperatures, contact times from about 6 up to about 400 minutes may be employed. When a continuous process is contemplated, pressures of from 25 to 10,000 psig. may be employed, with 25 to 1,000 psig preferred. The pressures stated are advantageously achieved by the use of nitrogen or other inert gas with varying degrees of an autogenous pressure contribution from the reaction system. The process is quite satisfactorily conducted under autogenous pressure alone.

A volatile inert highly-polar organic solvent may be employed if desired, particularly if a batch process is contemplated. The use of a solvent is especially advantageous when higher-boiling ketone reactants are used. It is frequently desirable, in both the batch and continuous embodiments, to employ a portion of the specific  $\beta,\beta$  - disubstituted -  $\beta$  - cyano-ketone product concerned in the present method as a solvent. Suitable solvents include dimethylformamide, dimethylacetamide, 1-methyl - 2 - pyrrolidinone, 1,5 - dimethyl - 2-pyrrolidinone, and 1,3-dimethyl-2-imidazolidinone.

An alkaline catalyst capable of generating cyanide ions is required and is preferably used in amounts of about 0.1 to 20% by weight of the total weight of the reactants. Suitable in this respect are alkali metals and their carbonates; alkali and alkaline earth metal lower alkoxides, oxides, hydroxides, peroxides, and cyanides; *tert*-amines; and quaternary ammonium bases. Actually, there may be employed as catalyst any base which has an ionization constant above about  $10^{-7}$  when determined in an aqueous medium. Typical examples of the catalyst that may be used include sodium, potassium, lithium, sodium methoxide, potassium butoxide, lithium ethoxide, magnesium ethoxide, sodium oxide, potassium hydroxide, calcium oxide, barium hydroxide, strontium hydroxide, sodium peroxide, magnesium peroxide, potassium cyanide, lithium cyanide, barium cyanide, magnesium cyanide, sodium carbonate, potassium carbonate, trimethylamine, triethylamine, triethanolamine, octyldimethylamine, N-methyl-

morpholine, benzyltrimethylammonium hydroxide, dibenzyltrimethylammonium hydroxide and dodecyltrimethylammonium hydroxide. The alkali metal cyanides are particularly effective for the instant purposes.

Yields of about 70 to 96% and above are consistently achieved, with the higher yields obtained when a continuous operation is used. Under the reaction conditions described herein, there is substantially no polymerization of the hydrocyanic acid and there are substantially no cyclization, condensation, or decomposition compounds formed, either or both of which undesired results frequently plague the cyanation procedures known to the art.

In a practical way of carrying out the process of the invention, whether the continuous or batch embodiment is used, the catalyst and a portion of the ketone reactant is initially charged to the reaction vessel and to this mixture there is then gradually added a mixture of the same ketone reactant and hydrocyanic acid. Alternatively, it is possible to use as an initial charge to the reaction vessel a mixture of the catalyst with a portion of the ketone nitrile product from a previous run, to this mixture being added a mixture of hydrocyanic acid and ketone reactant. By employing, as part of the initial charge, the ketone reactant or the ketone nitrile product, the formation of undesired condensation products is reduced to a minimum or entirely eliminated. This leads to maximum yields with minimum amounts of undesired products, which minimizes or substantially eliminates problems of separation and isolation of the product. It is also satisfactory in the present invention, when either a batch or continuous embodiment is used, to add all of the catalyst mixture at the beginning of the reaction or intermittently, as desired. It should be particularly noted that the hydrocyanic acid mixture may not be added all at once. Thus, as previously indicated, the hydrocyanic acid mixture is gradually brought into contact with the catalyst mixture at a rate which is substantially that at which the hydrocyanic acid reacts with the ketone. This prevents the build-up of hydrocyanic acid which, if present in a large amount at any one time, favours undesired polymerization reactions.

In some cases, it may be that the catalyst is not soluble or at least not entirely soluble in the reaction system, and it is, therefore, desirable to employ agitation such as stirring or rocking or the like in order to ensure the highest activity from the catalyst. Agitation of the reaction system is generally advantageous.

At the conclusion of the reaction, the catalyst may be neutralized by the addition of acid, preferably of a mineral acid such as phosphoric, sulfuric or hydrochloric. The reaction mixture may then be filtered, if desired, and then distilled, preferably at reduced pressures. The products are colorless liquids and are

useful as insecticides and as solvents for polymers. The products are particularly useful against the red spider and the rice weevil. They apparently are more effective against the red spider when employed as a spray in an inert hydrocarbon solvent base. The compounds are preferably used against the rice weevil in the form of a 10% dust in an inert commercial base. The compounds prepared according to the invention may also be used as fungicides, particularly against *Stemphylium sarcinaeforme* and *Monilinia fructicola*, especially in percentages approaching 1% of product in an inert base.

The present invention may be more fully understood from the following examples, which are offered by way of illustration and not by way of limitation. Parts by weight are used throughout.

#### EXAMPLE 1

There are added to a stainless steel autoclave equipped with heating jacket, pressure gauge, thermometer well, blow-out disc, vent valve, and feed line made of copper pressure tubing 639 parts of mesityl oxide and 29.3 parts of powdered potassium cyanide. The autoclave is sealed and heated to 135° C. while maximum stirring speed is employed. In about one hour, the resultant autogenous pressure is 30 psig. A mixture of 243 parts of mesityl oxide and 216 parts of hydrocyanic acid is then poured into the reservoir of the pressure feed system and pressurized to 30 psig. with nitrogen gas. The hydrocyanic acid-mesityl oxide mixture is then pumped into the autoclave at a rate of about six parts per

minute. During this addition, the temperature is maintained at 135° to 143° C. and the pressure increases from 30 to 55 psig. There is then added an additional 10 parts of mesityl oxide to rinse out the feed lines and then the reaction mixture is stirred at maximum speed for 0.25 hour at 135° to 140° C. The autoclave is then cooled by means of an ice-bath and, when the temperature of the mixture reaches 30° C., the autoclave is vented and emptied. The reaction mixture is neutralized by the addition of 12.5 parts of aqueous 85% phosphoric acid. The mixture is then distilled under reduced pressure and the product is isolated at 82° C. at 4.0 mm. absolute pressure. The product, which melts at 12° C. and boils at 222° C. at atmospheric pressure, has an  $n_D^{25}$  value of 1.4720 and contains 11.10% nitrogen (11.20% nitrogen theoretical).

The product shows a peak in the infrared absorption spectrum at 2265  $\text{cm}^{-1}$ , which is characteristic of an unconjugated nitrile function. It further shows a peak at 1730  $\text{cm}^{-1}$ , which is characteristic of a ketonic carbonyl group. The product is identified as mesitono-nitrile.

In a similar manner, the above product is obtained by employing magnesium cyanide, triethylamine, triethanolamine, and dibenzyl-dimethylammonium hydroxide, respectively, as catalysts.

The above reaction is repeated, with similar results, employing various temperatures, pressures, and reaction times as shown in Table I.

TABLE I

Temp. Range, °C.	Pressure Range Psig.	Reaction Time, Hrs.	% N	Product $n_D^{25}$	Conversion %	Yield %
127—170	Atmospheric	7.5	11.05	1.4289	29.2	41.2
100—106	12—49	1.6	11.17	1.4290	20.0	68.1
136—139	18—41	3.25	11.13	1.4282	72.4	85.9
135—141	15—51	1.7	11.14	1.4275	59.0	87.1
130—142	30—65	1.25	11.30	1.4270	62.8	89.1
135—140	30—55	2.0	11.12	1.4270	67.8	91.9

The data in Table I in respect of the first two runs, which were not carried out under the conditions required in the process of the invention, are included for comparative purposes. The increased yields obtained in the last four runs employed using reaction conditions according to the invention are immediately apparent.

#### EXAMPLE 2

A stainless steel autoclave is charged with 100 parts of mesitono-nitrile and 21.5 parts of potassium cyanide. The autoclave is then sealed and pressurized to 50 psig. with nitrogen. The stirring is started and the autoclave heated to

- 200° C. in about seven minutes' time. A mixture of 2062.5 parts of hydrocyanic acid and 4459 parts of mesityl oxide is then added to the autoclave at a rate of about 15.9 parts per minute. When the volume of the reaction mixture reaches about 200 ml., the take-off of product is started, with the output of product adjusted approximately to equal the input of reactants. The contact time is 11.3 minutes. The temperature during the run is maintained at 225° to 240° C., and the pressure is maintained at 70 to 150 psig. At the conclusion of the reaction, the product mixture is neutralized by the addition of aqueous 85% phosphoric acid. The product is isolated by distillation at 82° C. at 4.0 mm. absolute pressure. The product contains 11.1% nitrogen (theoretical 11.2% nitrogen) and has an  $n_D^{25}$  value of 1.4278. It is identified as mesitonitrile. The yield is 92% based on unrecovered mesityl oxide.
- In a similar way, there is prepared 3,4-dimethyl - 4 - cyanopentan - 2 - one by employing 3,4 - dimethyl - 3 - penten - 2 - one as a reactant in the presence of a sodium methoxide catalyst.
- The above continuous process for the preparation of mesitonitrile is repeated, employing various temperatures, pressures, and contact times as shown in Table II.

TABLE II

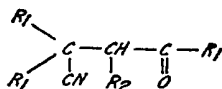
Temp. Range, °C.	Pressure Range Psig.	Contact Time Minutes	Product		Conversion %	Yield %
			% N	% purity		
135—152	10—80	23	11.10	99.1	22.7	65.0
147—157	75—125	25	11.04	94.4	57.3	66.8
166—174	0—100	12	11.05	98.7	46.8	85.9
190—207	30—105	12	11.02	98.4	76.8	83.4
225—233	100—160	6	11.01	98.3	68.9	80.4
223—230	100—175	12	10.95	97.3	84.2	90.2
230—233	105—170	12	11.10	99.1	79.3	89.6
225—240	70—150	12	11.11	99.2	85.6	91.6
225—240	25—175	10	11.10	99.1	86.3	95.1

- The data given in Table II above in respect of the last four runs indicate the high yield obtainable using a continuous process at temperatures in the range from 200° to 240° C. and contact times of 10 to 12 minutes.

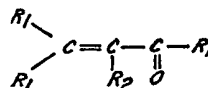
In conclusion, by reason of Section 9 of the Patents Act 1949, reference is directed to United Kingdom Patent No. 730,209.

#### WHAT WE CLAIM IS:—

1. A process for the preparation of a  $\beta,\beta$ -disubstituted- $\beta$ -cyanoketone of the formula:



- by the hydrocyanation of a  $\beta,\beta$ -disubstituted- $\alpha,\beta$ -unsaturated ketone of the formula:



where, in the above formulae,  $R_1$  represents a methyl or ethyl group,  $R_2$  represents hydrogen or a methyl or ethyl group, the  $R_1$  substituents being the same or different and the  $R_1$  and  $R_2$  substituents being such that the nitrile product contains from 7 to 9 carbon atoms, which process comprises bringing together, at the reaction temperature, preformed mixtures of (a) an alkaline catalyst capable of generating cyanide ions and said  $\alpha,\beta$ -unsaturated ketone reactant or the desired cyano-ketone product and (b) hydrocyanic acid and said  $\alpha,\beta$ -unsaturated ketone reactant, gradually bringing the hydrocyanic acid mixture

- (b) into contact with the catalyst mixture (a) at a rate which is substantially that at which the hydrocyanic acid reacts with the ketone, and carrying out the reaction at a super-atmospheric pressure and a temperature which is at least 130°C. but which does not exceed 350°C.
2. A process according to Claim 1 carried out by initially charging to a reaction vessel said catalyst mixture (a) and then gradually adding thereto the hydrocyanic acid mixture (b).
3. A process according to Claim 1, carried out in a batchwise fashion at a temperature from 130° to 275°C.
4. A process according to Claim 1, carried out in a batchwise fashion at a temperature in the range from 130° to 220°C.
5. A process according to Claim 3 or 4, carried out under a pressure of 25 to 250 psig.
6. A process according to Claim 1, carried out in a continuous fashion.
7. A process according to Claim 6, carried out with a contact time of 10 to 20 minutes.
8. A process according to Claim 6, carried out at a temperature from 200° to 240°C. with a contact time of 10 to 12 minutes.
9. A process according to any one of Claims 6—8, carried out under a pressure of 25 to 1000 psig.
10. A process according to any one of the preceding claims in which the reaction is carried out in the presence of a volatile inert highly polar organic solvent.
11. A process according to any one of the preceding claims in which the catalyst is an alkali metal cyanide.
12. A process according to any one of the preceding claims in which the catalyst is present in an amount of 0.1 to 20% by weight of the total weight of reactants.
13. A process according to any one of the preceding claims as applied to the preparation of mesitonitrile from mesityl oxide.
14. A process according to Claim 3, carried out substantially as hereinbefore described with reference to Example 1.
15. A process according to Claim 6, carried out substantially as hereinbefore described with reference to Example 2.
16. A  $\beta,\beta$  - disubstituted -  $\beta$  - cyanoketone whenever prepared by a method according to any one of the preceding claims.

For the Applicants,  
D. YOUNG & CO.,  
Chartered Patent Agents,  
9, Staple Inn, London, W.C.1.

